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# FORMULATION AND EVALUATION OF NANOSPONGES HYDROGEL FOR TOPICAL DRUG DELIVERY CONTAINING GRISEOFULVIN

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***ABSTRACT***

***The objective of the present study was to formulate Griseofulvin nanosponges hydrogel for topical delivery to treat topical fungal infection. Conventional dosage forms of Griseofulvin are available, but they show variation in bioavailability and they are associated with a number of toxicities when administered orally. To overcome these problems, the inclusion of Griseofulvin in topical gel formulation was approached with the aim of increasing permeability at the site of action which leads to improvement in bioavailability. The compatibility study of drug polymers and excipients was checked by FTIR studies. The Six formulations of nanosponges are formulated successfully using ethyl cellulose polymer and PVA as surfactant by using emulsion solvent diffusion method. The obtained nanosponges have been evaluated for particle size, zeta potential, XRD, surface morphology, entrapment efficiency, in-vitro drug release and stability studies. The scanning electron microscopy of nanosponges showed that Nanosponges are spherical in shape. Entrapment efficiency and in-vitro diffusion of optimized F5 formulation was found to be 73% to 93% respectively. The prepared nanosponges were formulated to hydrogels by simple dispersion method using carbopol 934 as a gelling agent and propylene glycol as permeation enhancer. Formulated hydrogel are evaluated for visual appearance, pH, spreadability, assay, and in vitro permeation. The evaluation results of Griseofulvin loaded nanosponges hydrogel show that G2 formulation increasing the solubility and permeability of poorly water soluble drug i.e. Griseofulvin.***

***KEYWORDS: Griseofulvin, Nanosponges, Hydrogel, Emulsion Solvent Diffusion Method & Zeta Potential***

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Original Article

## 1. INTRODUCTION

Targeted drug delivery system has been the major problem of medical researcher is, “how to target them to the right place in the body?” and “how to manage the release of the drug?” to prevent overdose. The developments of new molecule like Nanosponges have the potential to solve these problems. Nanosponges are small sponges – like porous particular structure in which a large variety of substances can be encapsulated or suspended, and then be included into a dosage form. They have a spherical colloidal character; have a very high solubilization capability for poorly soluble drugs by their inclusion and non-inclusion behavior. Nanosponges have recently been developed and useful for drug delivery. Nanosponges can solubilize into poorly water soluble drug not only provide prolonged release but also improved drug bioavailability. Nanosponges are able to load both hydrophilic and hydrophobic drug molecules because of their inner hydrophobic cavities and external hydrophilic branching, thereby offering breathtaking flexibility. Nanosponges are further like a 3D network or scaffold which consist of the backbone is

know as long length polyester which is mixed in solution with crosslinkers that act like tiny hooks to fasten different parts of the polymer together.

Griseofulvin is an antifungal substance obtained from the growth of certain strains of fungi i.e. Penicillium Griseofulvum. It is beneficial in fungal skin infections have been reported with some topical formulations. Griseofulvin band of activity is limited to dermatophytes and possesses a prolonged power needy transport system for the antibiotic. In case of topical drug delivery, the diffusion take place through the stratum corneum (lipoidal barrier) and drug allows different path to permeate through stratum corneum. Owing to poor aqueous solubility of griseofulvin, it cannot permeate across the skin barrier. In the current study, an attempt has been made to formulate griseofulvin nanosponges and to incorporate the prepared nanosponges in the hydrogel for the topical drug delivery system.

## 2. MATERIALS AND METHODS

### 2.1 Materials

Griseofulvin obtained as gift sample from Rajesh Chemicals, Mumbai; Ethyl cellulose, Poly vinyl alcohol, Carbopol 934, Triethanolamine, Propylene glycol and dichloromethane from Meher Chemie, Mumbai.

### 2.2 Methods

#### 2.2.1 Drug Characterization

**a) Preformulation**

- **Physical Characteristics**

By visual examination, the drug was identified for physical characters like colour, texture.

- **Melting Point**

Small amount of drug was filled in an capillary tube where one end of capillary was closed and kept in melting point apparatus and temperature was noted when drug melts.

- **Solubility Studies**

Solubility of Griseofulvin was studied in distilled water, organic solvents and phosphate buffer.

**b) FTIR Analysis**

FTIR was used to find whether any kind of interaction between drug and polymer exists. IR spectra for nanosponges were taken separately to know the interactions. Samples were mixed with KBr powder to make pellets by applying 5 ton pressure. By powder diffuse reflectance on FTIR; spectra were obtained at an ambient temperature using PerkinElmer Spectrum Version 21. The scanning range used was from 4000-400 $cm^{-1}$ at a scan period of 3 min.

**c) UV Spectrophotometric Analysis**

UV-visible spectrophotometer was used to determine the maximum absorbance (λ-max) of griseofulvin using a digital double - beam recording spectrophotometer with scanning range of 200-400 nm. Solution of griseofulvin was prepared using double distilled water. Shimadzu UV visible spectrophotometer (Perkin Elmer, Lambda 35 Model) 1800 with spectral bandwidth of 1 nm ± 0.3 nm wavelength accuracy and 10 mm pair of quartz cells were used to record the spectral and absorbance readings. UV spectrum was represented in graph.

### 2.2.2 Nanosponges Preparation

The six different nanosponge formulations (Table 1) are formulated by using emulsion solvent dispersion method. Firstly, ethyl cellulose was dissolved in 20 ml of dichloromethane and griseofulvin was added and agitated by using magnetic stirrer to dissolve. This was considered as organic internal phase. Then organic internal phase was added drop by drop using 100 ml syringe to aqueous external phase which contained PVA (200 to 300 mg) in 100 ml distilled water and stirred for 2 hr using magnetic stirrer at 1000 rpm. The resultant dispersion was filtered, desiccated for 24 hr at 40˚c and the powder obtained was used for characterization.

**Table 1: Formulation Table of Nanosponges**

| Ingredients | Formulations | | | | | |
|---|---|---|---|---|---|---|
| | F1 | F2 | F3 | F4 | F5 | F6 |
| Griseofulvin (mg) | 100 | 100 | 100 | 100 | 100 | 100 |
| Ethyl cellulose (mg) | 200 | 200 | 300 | 300 | 400 | 400 |
| Polyvinyl alcohol (mg) | 200 | 300 | 200 | 300 | 200 | 300 |
| Dichloromethane (ml) | 20 | 20 | 20 | 20 | 20 | 20 |
| Distilled Water (ml) | 100 | 100 | 100 | 100 | 100 | 100 |

### 2.2.3 Development of Nanosponges Hydrogel

Nanosponges hydrogel (Table 2) are prepared using simple dispersion method. In this, gel forming polymer i.e. carbopol soaked in water for 2 hr and dispersed using magnetic agitation at ≅ 600 rpm with the help of magnetic stirrer to get smooth dispersion. The stirring was stopped and dispersion was allowed to stand for 15 min to expel entrapped air. To this aqueous solution, triethanolamine (2 % w/v) was added with agitation. Finally ethanolic solution of nanosponges and propylene glycol was added in to the prepared base.

**Table 2: Formulation Table of Nanosponge Based Gel**

| Ingredient | G1 | G2 | G3 |
|---|---|---|---|
| GF NS | 100 mg | 100 mg | 100 mg |
| Carbopol 934 | 0.5 gm | 1 gm | 1.5 gm |
| Triethanolamine | 2 ml | 2 ml | 2 ml |
| Propylene glycol | 10 ml | 10 ml | 10 ml |
| Distilled water | 100 ml | 100 ml | 100 ml |

## 3. EVALUATION METHODOLOGY

### 3.1 Nanosponge

### 3.1.1 Percentage Yield

The percentage yield of nanosponge have calculated by weighing the final weight of nanosponges and the initial weight of drug with excipients used for the preparation of nanosponges, i.e. weight of drug, polymer and other excipients employed in the preparation. Percentage yield of nanosponges calculated using formula

$$\%Yield = \left\{\frac{Actual\ weight\ of\ nanosponge\ prepared}{Weight\ of\ Drug + Weight\ of\ polymer + Weight\ of\ cross\ linker}\right\} \times 100$$

### 3.1.2 Entrapment Efficiency

The drug loaded nanosponges have centrifuged at a high speed of 9000 rpm for 30 min and the supernatant liquid was analyzed for non-bound drug in UV spectrophotometer at 291 nm. Then percentage encapsulation efficiency calculated

using formula,

$$\%EE = \left\{\frac{Drug\ added - Free\ unentrapped\ drug}{Drug\ added}\right\} \times 100$$

**3.1.3 Assay**

About 10 mg equivalent of griseofulvin nanosponges have diluted to 100 ml with phosphate buffer solution having pH 6.4. 1 ml aliquot from above solution was further diluted up to 10 ml to prepare 10 µg/ml concentration, which is analyzed using validated UV spectrophotometric method.

**3.1.4 Particle size and Polydispersity Index Analysis**

The average particle size and polydispersity index (PI) of the formulated nanosponges was determined by dynamic light scattering. Using Malvern Zetasizer, Malvern Instruments Ltd. United Kingdom, (Zetasizer Ver. 6.34 Serial Number: MAL1045544) the experiment was performed at 25 °C using clear disposable zeta cell, water as a dispersant which has refractive index (RI) - 1.330 and viscosity of 0.88 Cps. All the samples analyzed for three times to minimize the error.

**3.1.5 X-ray Diffraction (XRD)**

The X-ray diffraction (XRD) patterns of samples were recorded using Rigaku MiniFlex X-ray Desktop diffractometer with Kb filtered radiation was used (Cu Target). Samples were scanned at range of 2 θ from approximately 5° to 40°. The scanning speed used for the recording was 5/min with step size of 0.02 and the unit cell parameters (a, b, c & a, b, y) from the X-ray diffraction, data were determined using "Treor90" program provided by IIT, Bombay.

**3.1.6 Microscopy Study**

Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM) technique was used to study the microscopic behaviour of the drug, nanosponges and drug-nanosponges composite. The difference in crystallization situation of the raw materials and the product seen under electron microscope indicates that formation of inclusion complexes.

**3.1.7 *In vitro* Permeation**

*In vitro* permeation was carried out on jacketed vertical glass Franz diffusion cells (with the 15 ml of acceptor compartment volume) using dialysis membrane (mol. wt. 12000-14000) with effective surface area of 3.14 $cm^2$.

The mounting of the membrane was done by placing circular rubber above the permeation barrier and in between the acceptor and donor compartment and supported with clips at the rim of the compartments to avoid leakage of the test sample. The temperature of the receiver compartment having phosphate buffer solution maintained at 37 ± 1°C under continuous stirring with teflon coated magnetic bar at constant rate, in such a way that the dialysis membrane surface just flushes the phosphate buffer solution. Membrane was allowed to stabilize in both the compartment for 15 minutes with continuous stirring on magnetic stirrer. After 15 min; stabilized nanosponges (equivalent of 10 mg griseofulvin) have added in donor compartment. Samples are withdrawn at predetermined time intervals from sampling port of acceptor compartment and replaced with the fresh buffer media. The aliquots were diluted suitably and analyzed using validated UV method and concentration of drug permeated was determined. Studies have carried out for 24 hr (every hr till 12 hrs then at 24 hrs directly).

## 3.2 Gel

### 3.2.1 pH

For pH determination, digital pH meter was used. 10 % gel solution is prepared by dispersing about 2.5 gm of nanosponge based gel in 25 ml volume of water. This solution is exposed to digital pH meter.

### 3.2.2 Spreadability

It is assessed by glass slide and wooden base block apparatus. For determining spreadability, the gel sample spread in between two slides and have compressed to a uniform thickness by employing 1000 gm weight for a time period of 5 minutes. Weighed about 45 gm added to the pan. Time required to separate the slides from each other is known as spreadability. Spreadability calculated using formula,

$$S=ML/T$$

Where, S = Spreadability,

M = Weight applied upon the upper slide,

L = Length moved on the glass slide,

T = Time utilized to separate the slide from each other.

### 3.2.3 Homogeneity

By visual examination of all gel formulations gel is observed for presence of any lump particles, air entrapment or free from them.

### 3.2.4 Viscosity

Viscosity of nanosponge based gel is measured using Brookfield viscometer with 'Rheocal software'.

### 3.2.5 Comparative *in vitro* Permeation

*In vitro* permeation of GF (plain drug), GF gel (marketed formulation), optimized NS and GF NS HG was carried out by same procedure explained above and compared for GF diffusion or release. Data analysis of all these formulations was done and compared by using above equations.

### 3.2.6 Stability Studies

Optimized formulation subjected to accelerated stability study for 3 months as per ICH guidelines with temperature 40$\pm$ 2°C and relative humidity 75 $\pm$ 5% conditions. Formulations were analysed at 1, 2 and 3 months for following tests:

- Visual appearance
- pH
- Spreadability
- Assay
- *In vitro* permeation

## 4. RESULTS AND DISCUSSIONS

### 4.1 Physical Appearance

The sample of griseofulvin received was studied for its organoleptic characters such as color, odor, and appearance as it is one of the first criteria for identification of compound and it shows properties which comply to standards (Table 3).

**Table 3: Physical Appearance**

| Sl. No. | Properties | Observation |
|---|---|---|
| **1** | Visual appearance | Crystalline powder |
| **2** | Colour | White to pale cream colour |
| **3** | Odor | Odorless |

### 4.2 Melting Point

According to IP melting point of a substance is defined as those points of temperature at which the substance begins to melt and is completely melted except as defined otherwise for certain substances. The melting point of pure griseofulvin was found to be 220-223°C. The reported melting point of griseofulvin is 220 °C. Confirmation of melting point indicates the purity of sample.

### 4.3 Solubility Studies

According to standard specified; Griseofulvin is very slightly soluble in water (0.2 g/L at 25 °C); sparingly soluble in ethanol and methanol; soluble in acetone, chloroform and dimethyl formamide. Solubility study of drug sample was studied in different types of solvent and data shows that drug was very slightly soluble in Ethanol, Chloroform, Methanol, Acetic acid and freely soluble in N, N-Dimethyl formamide.

**Table 4: Solubility Study**

| Sl. No. | Solvent | Observation |
|---|---|---|
| **1** | N, N-Dimethyl formamide | Freely soluble |
| **2** | Ethanol, Chloroform, Methanol, Acetic acid | Slightly soluble |
| **3** | Water, Petroleum ether | Practically insoluble |

### 4.4 FTIR

FTIR spectra of pure GF are reported at wave numbers 1708, 1660, 1619, 1587, 1505, 1470, 1428, 1363, 1277, 1248, 1187, 1153, 1064, 1062, 961, 889, 822, 801 and 682 $cm^{-1}$. Similar peaks were observed in FTIR spectra of GF at wave numbers 1705.87, 1657.80, 1616.61, 1584.52, 1504.44, 1474.16, 1426.92, 1369.45, 1283.46, 1251.15, 1192.80, 1154.59, 1071.24, 1062.67, 959.48, 889.74, 821.12, 800.10 and 680.45 $cm^{-1}$.

In this FTIR spectra of GF, characteristic peak at wave number 680.45 $cm^{-1}$ indicates presence of benzene derivative, 1369.45 $cm^{-1}$ indicates O-H bend of aromatic ring, 1283.46 $cm^{-1}$ indicates C-O stretch of alkyl aryl ether, sharp peak at 889.74 and 821.12$cm^{-1}$ indicates C-Cl stretch of chloro-benzene ring, peak at 1705.87, 1657.80 $cm^{-1}$ indicates C=O stretch of lactum and three peaks at 1616.61, 1584.52 and 1504.44 $cm^{-1}$ indicates C=C stretch of aromatic ring.

Occurrence of only expected peaks for functional group at their respective wave number assured the purity of GF.

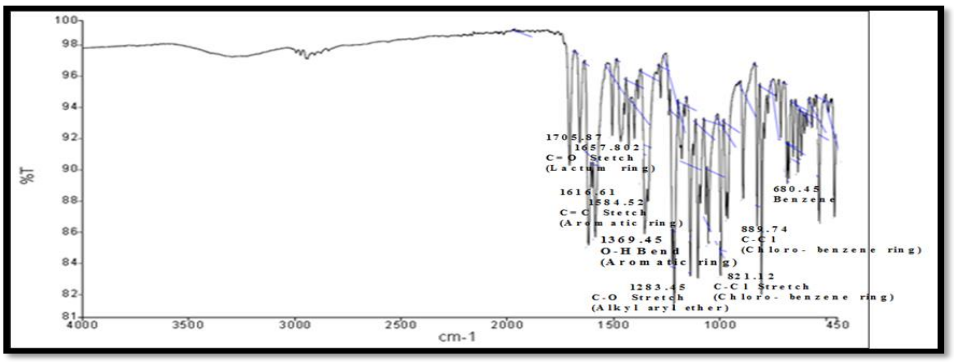


**Figure 1: FTIR Spectra of GF.**

### 4.5 Calibration Curve

The UV absorbance of Griseofulvin standard solutions in the range of 2-10 µg/ml of drug in buffer pH 6.4 showed linearity at λmax 291 nm. The absorbance values and standard curve presented in figure 2.

**Table 5: Absorbance of Drug on UV**

| Concentration of Drug (µg/ml) | Absorbance at 291 nm |
|---|---|
| 0 | 0 |
| 2 | 0.496 |
| 4 | 0.595 |
| 6 | 0.671 |
| 8 | 0.762 |
| 10 | 0.825 |

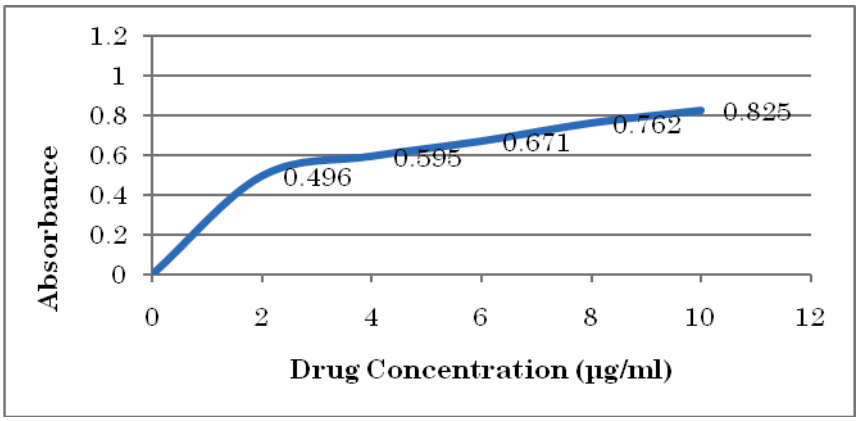


**Figure 2: Standard Calibration Curve.**

### 4.6 Evaluation of Nanosponge

**Table 6: Entrapment Efficiency, % Yield, Assay and Particle Size of All Nanosponge Batches**

| Batch | Entrapment Efficiency (%) | Yield (%) | Assay (%) | Particle size (nm) |
|---|---|---|---|---|
| F1 | 73.45 | 79.48 | 100.23 | 145.27 |
| F2 | 79.59 | 83.67 | 99.63 | 233.67 |
| F3 | 84.77 | 79.86 | 100.05 | 262.37 |
| F4 | **90.78** | **86.82** | 98.42 | 263.34 |
| F5 | **93.49** | **87.73** | 99.97 | 227.24 |
| F6 | 89.43 | **90.14** | 97.85 | 277.87 |

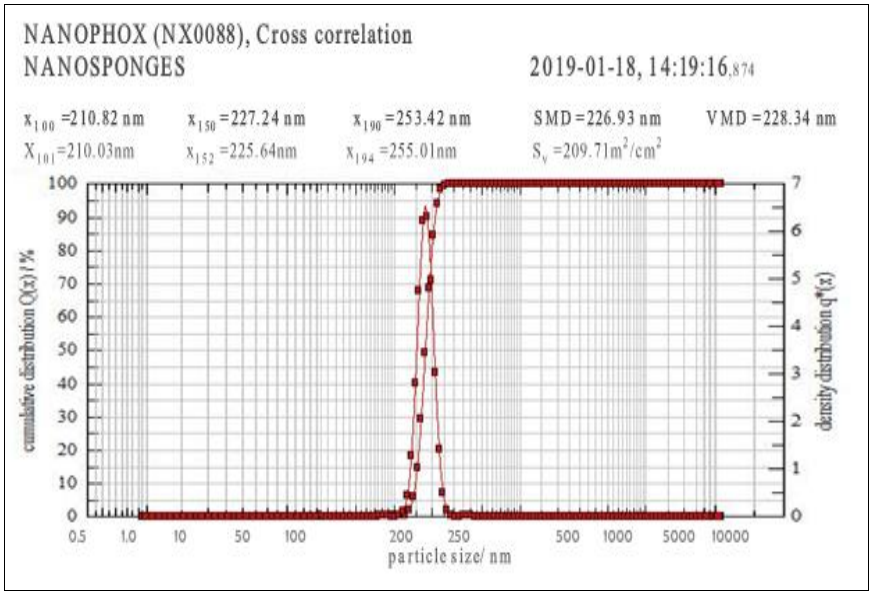


**Figure 3: Particle Size Analysis of Optimized Batch F5.**

### 4.7 X-Ray Diffraction Analysis

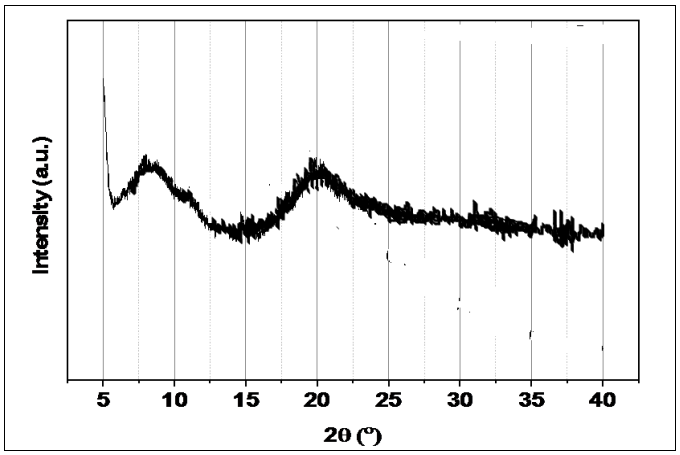


**Figure 4 (a): X- ray Diffractogram of Pure Drug.**

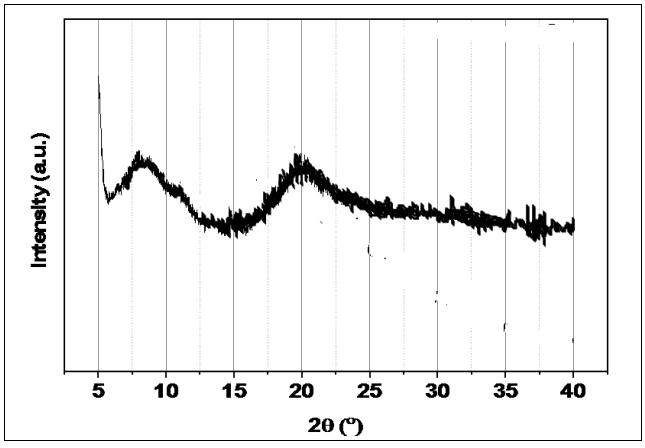


**Figure 4 (b): X- ray diffractogram of GF Nanosponge.**

4.8 **Microscopy**

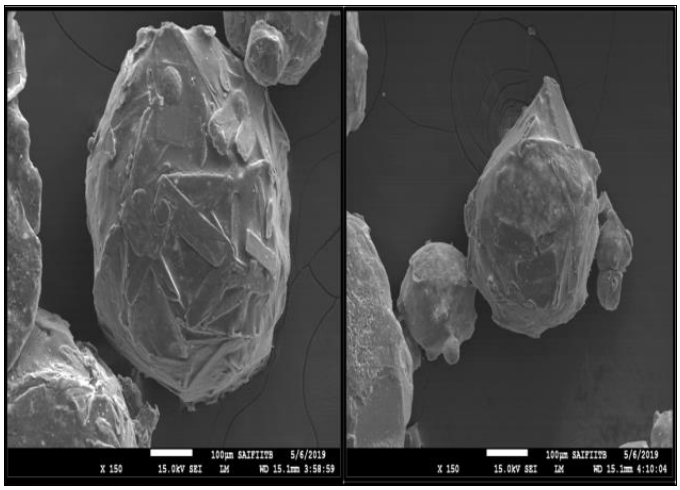

**Figure 5: SEM Photographs Showing Surface Morphology of F5.**

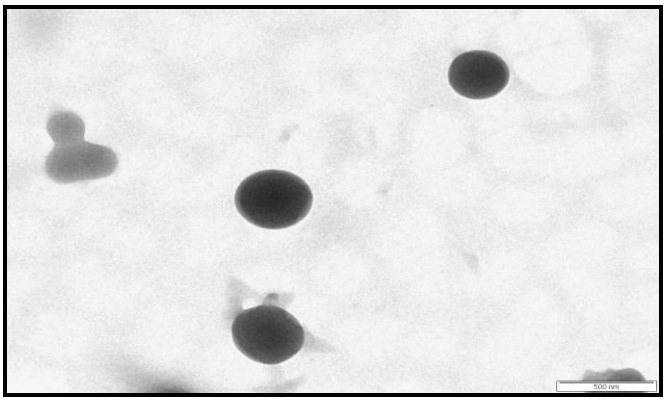

**Figure 6: TEM Photomicrography of Formulation F5 Nanosponges.**

**4.9 *In vitro* Permeation of Nanosponges**

**Table 7: In vitro Permeation of GF from different Batches of Nanosponges (n=3)**

| Time (hr) | Cumulative GF permeated through dialysis membrane (%) | | | | | |
|---|---|---|---|---|---|---|
| | $F_1$ | $F_2$ | $F_3$ | $F_4$ | $F_5$ | $F_6$ |
| **0** | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| **1** | 3.9 | 2.0 | 3.4 | 3.5 | 3.9 | 2.0 |
| **2** | 10.4 | 7.9 | 9.2 | 7.9 | 8.0 | 4.5 |
| **3** | 13.6 | 12.5 | 13.4 | 11.1 | 12.1 | 7.7 |
| **4** | 17.2 | 17.0 | 17.9 | 14.3 | 14.5 | 10.8 |
| **5** | 20.1 | 19.1 | 21.3 | 17.0 | 17.5 | 13.9 |
| **6** | 27.0 | 23.5 | 23.4 | 19.9 | 20.6 | 18.2 |
| **7** | 30.2 | 27.7 | 30.1 | 22.6 | 25.4 | 20.8 |
| **8** | 34.0 | 33.1 | 34.5 | 24.8 | 28.4 | 23.2 |
| **9** | 37.3 | 37.7 | 38.1 | 29.0 | 32.4 | 28.8 |
| **10** | 41.6 | 40.3 | 41.3 | 33.8 | 36.9 | 31.8 |
| **11** | 46.2 | 44.8 | 46.1 | 40.0 | 42.3 | 36.0 |
| **12** | 52.3 | 47.3 | 49.9 | 41.8 | 48.5 | 40.4 |
| **24** | 85.5 | 79.3 | 87.3 | 76.8 | **90.2** | 80.1 |

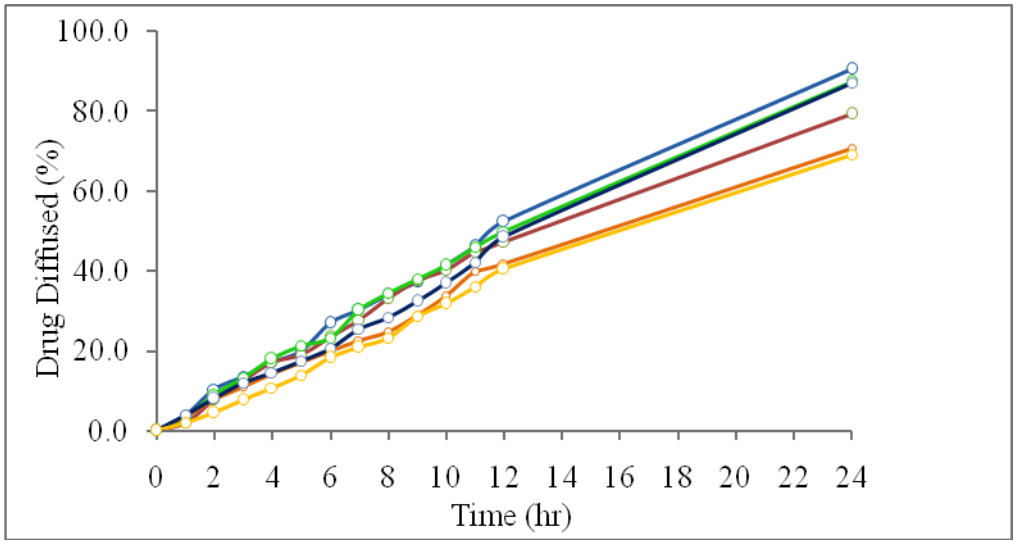


**Figure 7: Graph of % Drug Diffused vs Time in hr for all Batches (F1-F6).**

### 4.10 Evaluation of Nanosponge's Hydrogel:

**Table 8: Evaluation Results of Nanosponge Loaded Hydrogel**

| Formulation code | pH | Assay (%) | Viscosity (cps) | Spreadability (cm) | Gel strength* |
|---|---|---|---|---|---|
| G1 | 5.3±0.018 | 98.04% | 8.15±0.81 | 2.219±0.017 | + |
| G2 | 5.45±0.03 | 99.23% | 874±0.74 | 2.250±0.103 | ++ |
| G3 | 5.6±0.043 | 99.76% | 923±0.94 | 2.135±0.026 | +++ |

*+++ if time required is more than 4 h, ++ if time is 2.5-4 h and + if time is less than 2.5

### 4.11 In Vitro Permeation

*In vitro* permeation of griseofulvin loaded nanosponge hydrogel was carried out for 24 hr. The permeation was found to be 56.7- 68.0%.

**Table 9: In vitro Release of Nanosponge's Hydrogel**

| Time (h) | G1 | G2 | G3 |
|---|---|---|---|
| **0** | 0.0 | 0.0 | 0.0 |
| **1** | 1.2 | 1.6 | 1.1 |
| **2** | 2.4 | 2.8 | 3.7 |
| **3** | 2.3 | 6.6 | 5.4 |
| **4** | 4.2 | 10.0 | 9.6 |
| **5** | 4.6 | 11.9 | 10.7 |
| **6** | 12.6 | 16.1 | 13.8 |
| **7** | 17.3 | 20.5 | 18.7 |
| **8** | 21.0 | 22.5 | 21.5 |
| **9** | 23.7 | 25.8 | 24.8 |
| **10** | 28.4 | 31.2 | 29.1 |
| **11** | 35.6 | 35.5 | 33.3 |
| **12** | 42.4 | 40.3 | 36.1 |
| **24** | 65.7 | **68.0** | 56.7 |

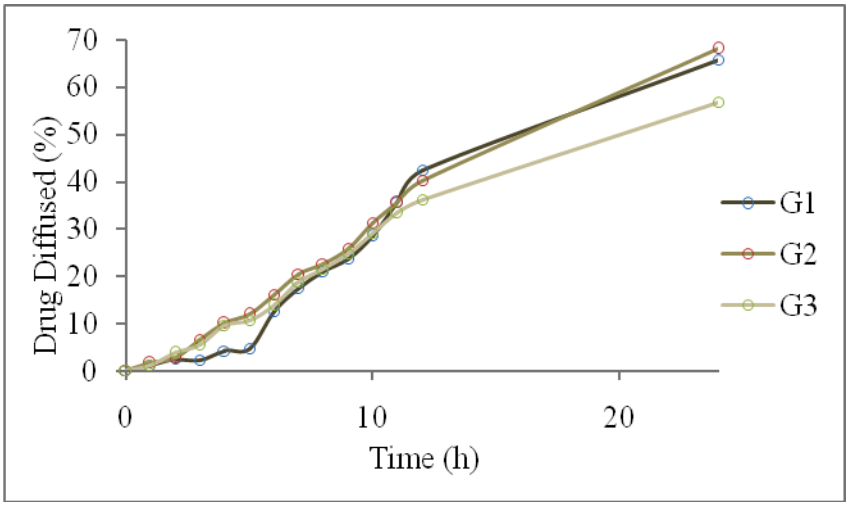


**Figure 8: Graph of in Vitro Permeation of all Nanosponge's Hydrogel Formulations.**

**Table 10: Comparative in Vitro Permeation Study Data in between Plain GF, GF gel, NS and NS HG**

| Time (hr) | Plain GF | GF gel | GF NS | GF NS HG |
|---|---|---|---|---|
| **0** | 0.0 | 0.0 | 0.0 | 0.0 |
| **2** | 2.1 | 1.3 | 11.7 | 2.8 |
| **3** | 2.6 | 2.0 | 15.4 | 6.6 |
| **4** | 3.4 | 2.8 | 19.6 | 10.0 |
| **5** | 4.3 | 3.5 | 28.7 | 11.9 |
| **6** | 5.1 | 4.2 | 33.8 | 16.1 |
| **7** | 6.0 | 4.9 | 38.7 | 20.5 |
| **8** | 6.6 | 4.9 | 42.5 | 22.5 |
| **9** | 7.7 | 5.6 | 47.8 | 25.8 |
| **10** | 8.4 | 6.8 | 54.1 | 31.2 |
| **11** | 9.6 | 7.7 | 63.3 | 35.5 |
| **12** | 12.4 | 8.5 | 72.1 | 40.3 |
| **24** | 21.7 | 17.1 | **89.7** | 68.**0** |

*GF= griseofulvin, NS= nanosponge, HG= hydrogel

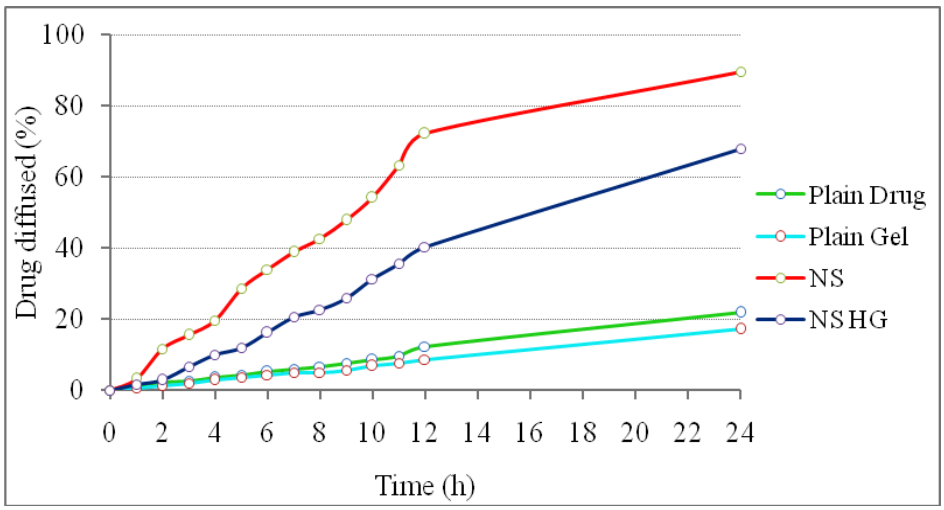


**Figure 9: Comparative In Vitro Permeation Graph Of Plain GF, GF Gel, NS And NS HG.**

### 4.12 Stability Study

**Table 11: Data Analysis of Stability Study of GF Loaded Nanosponges Hydrogel**

| Month | Temp. | Homogeneity | pH | Assay | Viscosity | Spreadability | Gel Strength |
|---|---|---|---|---|---|---|---|
| 1 | R.T. | No Change | 5.48 | 99.07 ±0.48 | 882 | 2.24 | ++ |
| | Acc. T. | No Change | 5.51 | 99.19 ± 0.27 | 898 | 2.33 | ++ |
| 2 | R.T. | No Change | 5.46 | 98.74 ±0.82 | 849 | 2.52 | ++ |
| | Acc. T. | No Change | 5.52 | 98.24 ±0.43 | 923 | 2.61 | +++ |
| 3 | R.T. | No Change | 5.52 | 97.52 ±0.55 | 901 | 2.58 | ++ |
| | Acc. T. | No Change | 5.58 | 96.89 ±0.64 | 931 | 2.67 | +++ |

**Mean ±SD (n=3),* +++ if time required is more than 4 hr, ++ if time is 2.5-4 hr and + if time is less than 2.5 hr

**Table 12: In Vitro Permeation of Optimized Hydrogel for 3 Months at RT and Acc. T (n=3)**

| Time (hr) | 1 month | | 2 month | | 3 month | |
|---|---|---|---|---|---|---|
| | RT | Acc. T | RT | Acc. T | RT | Acc. T |
| **0** | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| **1** | 3.9 | 3.0 | 4.1 | 2.3 | 3.5 | 2.9 |
| **2** | 10.7 | 9.8 | 11.4 | 8.5 | 10.8 | 7.9 |
| **3** | 14.8 | 14.2 | 15.0 | 13.4 | 16.4 | 13.4 |
| **4** | 18.4 | 19.7 | 20.1 | 19.2 | 21.6 | 18.6 |
| **5** | 21.7 | 23.3 | 27.4 | 24.7 | 26.5 | 25.3 |
| **6** | 28.5 | 29.4 | 31.8 | 30.2 | 30.8 | 29.5 |
| **7** | 31.7 | 33.7 | 34.1 | 33.3 | 34.2 | 32.4 |
| **8** | 35.2 | 36.0 | 38.2 | 37.5 | 39.9 | 37.5 |
| **9** | 42.9 | 41.8 | 42.3 | 42.4 | 44.1 | 41.8 |
| **10** | 46.9 | 45.8 | 47.3 | 45.4 | 49.1 | 44.8 |
| **11** | 49.6 | 48.2 | 52.2 | 48.0 | 53.2 | 47.3 |
| **12** | 53.1 | 51.6 | 57.5 | 50.1 | 56.3 | 49.1 |
| **24** | 67.3 | 66.1 | 70.8 | 65.8 | 68.9 | 63.1 |

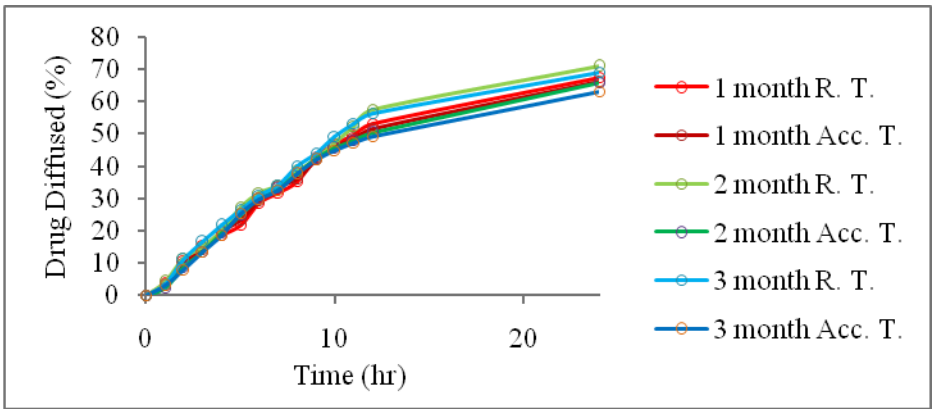


**Figure 10: In Vitro Permeation of Optimized GF NS Hydrogel for 3 Months at R. T. and Acc. T.**

## 5. CONCLUSIONS

The nanosponges prepared with ethyl cellulose, polyvinyle alcohol and dichloromethane were successfully incorporated into topical hydrogels. The polymer used in griseofulvin Nanosponges formulation show efficient and controlled drug

release. Nanosponges drug delivery show prolong drug release which is beneficial for chronic fungal infection. Additional benefits such as reduction in dose, dosing frequency and reduced side effects.

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